CLN6 disease

CLN6 disease is an inherited disorder that primarily affects the nervous system. The signs and symptoms of this condition typically begin between early and late childhood, but sometimes they can appear in adulthood.

Most children with CLN6 disease initially experience the loss of previously acquired skills (developmental regression). Affected individuals can also develop recurrent seizures (epilepsy), difficulty coordinating movements (ataxia), muscle twitches (myoclonus), impaired speech (dysarthria), and vision loss. The movement problems worsen over time until affected children cannot walk, stand, or sit without assistance. Intellectual function also declines over time. Most children with CLN6 disease do not survive into adulthood.

Some people with CLN6 disease do not show signs or symptoms of the condition until adulthood, typically after age 30. These individuals can have epilepsy, ataxia, dysarthria, and a progressive loss of intellectual function. CLN6 disease usually does not cause vision loss in affected adults. Adults with this condition do not often survive more than 10 years after diagnosis.

CLN6 disease is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs), which may also be collectively referred to as Batten disease. All these disorders affect the nervous system and typically cause worsening problems with vision, movement, and thinking ability. The different NCLs are distinguished by their genetic cause. Each disease type is given the designation "CLN," meaning ceroid lipofuscinosis, neuronal, and then a number to indicate its subtype.

Frequency

The incidence of CLN6 disease is unknown; more than 125 cases have been described in the scientific literature. Collectively, all forms of NCL affect an estimated 1 in 100,000 individuals worldwide.

Genetic Changes

Mutations in the *CLN6* gene cause CLN6 disease. The *CLN6* gene provides instructions for making a protein whose function is not well understood. Within cells, the CLN6 protein is found in a structure called the endoplasmic reticulum, which is involved in protein processing and transport. Research suggests that the CLN6 protein helps cells get rid of materials they no longer need.

Most *CLN6* gene mutations result in the production of an abnormal CLN6 protein that is quickly broken down (degraded). As a result, there is a severe reduction in the amount

of functional CLN6 protein in cells. While it is not known how the loss of this protein causes the signs and symptoms of CLN6 disease, it is likely that the protein's quick degradation contributes to the childhood onset of CLN6 disease.

In the cases in which CLN6 disease develops in adulthood, *CLN6* gene mutations often result in a CLN6 protein with reduced function. Research suggests that these *CLN6* gene mutations allow enough functional protein to be produced so that signs and symptoms of the disorder do not develop until later in life.

CLN6 disease, like other NCLs, is characterized by the accumulation of proteins and other substances in lysosomes, which are cell structures that digest and recycle different types of molecules. These accumulations occur in cells throughout the body; however, nerve cells seem to be particularly vulnerable to their effects. The accumulations can cause cell damage leading to cell death. The progressive death of nerve cells in the brain and other tissues leads to the signs and symptoms of CLN6 disease. However, it is unclear how mutations in the *CLN6* gene are involved in the buildup of substances in lysosomes in CLN6 disease. These accumulations occur in more cells throughout the body in children with CLN6 disease than in affected adults.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- ceroid lipofuscinosis neuronal 6
- CLN6-related neuronal ceroid lipofuscinosis
- neuronal ceroid lipofuscinosis 6

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Ceroid lipofuscinosis neuronal 6
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1866282/

Other Diagnosis and Management Resources

- GeneReview: Neuronal Ceroid-Lipofuscinoses
  https://www.ncbi.nlm.nih.gov/books/NBK1428
- MedlinePlus Encyclopedia: Neuronal Ceroid Lipofuscinoses (NCL)
  https://medlineplus.gov/ency/article/001613.htm
- University of Rochester Batten Center
  https://www.urmc.rochester.edu/neurology/batten-disease-center.aspx

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Neuronal Ceroid Lipofuscinoses (NCL)
  https://medlineplus.gov/ency/article/001613.htm
- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html

Genetic and Rare Diseases Information Center

- Neuronal ceroid lipofuscinosis 6
  https://rarediseases.info.nih.gov/diseases/1224/neuronal-ceroid-lipofuscinosis-6

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Batten Disease Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Batten-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page

Educational Resources

- Baylor College of Medicine: Myoclonus
  https://www.bcm.edu/healthcare/care-centers/parkinsons/conditions/myoclonus
- Disease InfoSearch: Neuronal Ceroid Lipofuscinosis
  http://www.diseaseinfosearch.org/Neuronal+Ceroid+Lipofuscinosis/5192
- MalaCards: neuronal ceroid lipofuscinosis
  http://www.malacards.org/card/neuronal_ceroid_lipofuscinosis_2
- Orphanet: Neuronal ceroid lipofuscinosis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=216
- The University of Arizona Health Sciences
  http://disorders.eyes.arizona.edu/disorders/neuronal-ceroid-lipofuscinoses
- University College London
  http://www.ucl.ac.uk/ncl/batten.shtml

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  http://aaidd.org/
- Batten Disease Family Association
  http://www.bdfa-uk.org.uk/variant-late-infantile-onset-ncls-cln5-cln6-cln7-and-cln8-diseases-others/
- Batten Disease Support and Research Association
  http://bdsra.org/
- Beyond Batten Disease Foundation
  http://beyondbatten.org/

GeneReviews

- Neuronal Ceroid-Lipofuscinoses
  https://www.ncbi.nlm.nih.gov/books/NBK1428

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22CLN6+disease%22+OR+%22Neuronal+Ceroid-Lipofuscinoses%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Neuronal+Ceroid-Lipofuscinoses%5BMAJR%5D%29+AND+%28CLN6%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- CEROID LIPOFUSCINOSIS, NEURONAL, 6
  http://omim.org/entry/601780

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  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631127/
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